Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/US05/003766

International filing date: 04 February 2005 (04.02.2005)

Document type: Certified copy of priority document

Document details: Country/Office: US
Number: 60/542,198
Filing date: 05 February 2004 (05.02.2004)

Date of receipt at the International Bureau: 15 July 2005 (15.07.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)

World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse

1343236

THE UNITED STATES OF AMERICA

TO ALL TO WHOM THESE PRESENTS SHALL COME:

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

July 09, 2005

THIS IS TO CERTIFY THAT ANNEXED HERETO IS A TRUE COPY FROM THE RECORDS OF THE UNITED STATES PATENT AND TRADEMARK OFFICE OF THOSE PAPERS OF THE BELOW IDENTIFIED PATENT APPLICATION THAT MET THE REQUIREMENTS TO BE GRANTED A FILING DATE.

APPLICATION NUMBER: *60/542,198*
FILING DATE: *February 05, 2004*
RELATED PCT APPLICATION NUMBER: *PCT/US05/03766*

Certified by

Jon W. Dudas

Under Secretary of Commerce
for Intellectual Property
and Director of the United States
Patent and Trademark Office

PTO/SB/16 (01-04).
Approved for use through 07/31/2006. OMB 0651-0032.
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

PROVISIONAL APPLICATION FOR PATENT COVER SHEET

This is a request for filing a PROVISIONAL APPLICATION FOR PATENT under 37 CFR 1.53(c).

Express Mail Label No. EL 999509502 US

INVENTOR(S)		
Given Name (first and middle [if any])	Family Name or Surname	Residence (City and either State or Foreign Country)
J. Kenneth	Hoober	Phoenix, Arizona

Additional inventors are being named on the 1 *separately numbered sheets attached hereto*

TITLE OF THE INVENTION (500 characters max)

Peptide Sugar Mimetic of N-Acetylgalactosamine for Use as a Potential Cancer and Pathogen Therapy

Direct all correspondence to: **CORRESPONDENCE ADDRESS**

☑ Customer Number: 39978

OR

☐ Firm or Individual Name					
Address					
Address					
City		State		Zip	
Country		Telephone		Fax	

ENCLOSED APPLICATION PARTS *(check all that apply)*

☑ Specification *Number of Pages* 3 ☐ CD(s), Number

☐ Drawing(s) *Number of Sheets* ☐ Other (specify)

☐ Application Data Sheet. See 37 CFR 1.76

METHOD OF PAYMENT OF FILING FEES FOR THIS PROVISIONAL APPLICATION FOR PATENT

☑ Applicant claims small entity status. See 37 CFR 1.27.

☐ A check or money order is enclosed to cover the filing fees.

☑ The Director is herby authorized to charge filing fees or credit any overpayment to Deposit Account Number: 501234

☐ Payment by credit card. Form PTO-2038 is attached.

FILING FEE Amount ($): $80.00

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☑ No.

☐ Yes, the name of the U.S. Government agency and the Government contract number are:

Respectfully submitted,

SIGNATURE

TYPED or PRINTED NAME Joseph W. Mott

TELEPHONE 602 262-5866

Date 02/04/2004

REGISTRATION NO. 35,621 *(if appropriate)*

Docket Number:

USE ONLY FOR FILING A PROVISIONAL APPLICATION FOR PATENT

This collection of information is required by 37 CFR 1.51. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 8 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop Provisional Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.

PROVISIONAL APPLICATION COVER SHEET
Additional Page

PTO/SB/16 (08-03)
Approved for use through 07/31/2006. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

Docket Number

INVENTOR(S)/APPLICANT(S)		
Given Name (first and middle [if any])	Family or Sumame	Residence (City and either State or Foreign Country)
Laura L.	Eggink	Scottsdale, Arizona
Valerie	Jacobs	Phoenix, Arizona

Number 1 of 1

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

PEPTIDE SUGAR MIMETIC OF *N*-ACETYLGALACTOSAMINE FOR USE AS A POTENTIAL CANCER AND PATHOGEN THERAPY

Laura L. Eggink, Valerie L. Jacobs and J. Kenneth Hoober

Rationale

Carbohydrate antigens are immune targets associated with a variety of pathogens and cancers. Lectin-carbohydrate interactions are required for macrophage-mediated toxicity toward these invaders. A human serum glycoprotein, human Vitamin D-Binding protein, with known macrophage activating activity, can be administered as a therapy against cancers and pathogens (1,2). Unfortunately, viruses and cancers produce glycosidases which cleave sugar moieties from natural and man-made therapeutic antigens and thereby inactivate the protein. Molecular mimics of carbohydrates presents a novel and stable alternative source of compounds to target pathways involving protein-carbohydrate interactions. Expected outcome: The peptide mimetic therapy will not require a *N*-acetylgalactosamine (GalNAc), which is difficult to produce and is easily inactivated. The peptide mimetic will have all the activity of human Vitamin D-Binding protein but will possess greater stability and ease of synthesis. Additionally, the sequence of the active site is novel and without homology to current patents held on Vitamin D-Binding protein.

Summary of the Invention

We have discovered a 12-mer peptide sequence that mimics a required GalNAc of a macrophage activating factor, as determined by binding to a GalNAc specific lectin. To increase stability and reactivity, this peptide may be fused to a protein carrier, such as the C-terminus of human Vitamin D-Binding protein. It has been previously shown that peptide sugar mimetics can induce functional carbohydrate cross-reactive immune

responses in pathogen and tumor models (3). Therefore, this fusion peptide is expected to be active in the therapeutic remission of cancer and biological inactivation of pathogen infection. Peptide mimetics also have an advantage in that they can be synthesized in prokaryotic organisms. Because of the novelty of this invention, a suite of patents may be filed in support of the peptide sugar mimetic, which may include intellectual property covering activity and delivery of the peptide. This cluster would provide an attractive portfolio to interested licensees.

Construction of GalNAc Peptide Mimetic

Combinatorial peptide libraries displayed on phage M13 provided approximately 3×10^9 variants of a 12-amino acid sequence. Each of these sequences were present in about 55 copies. The total library was screened with a GalNAc-specific lectin to search for a peptide mimetic of the sugar. Phage particles that bound to the lectin were eluted with free GalNAc and the process was repeated several times. After DNA of phage that were selected by this procedure were sequenced, a unique consensus amino acid sequence of VQATQSNOHTPR emerged. Insertion of variations of this sequence should allow construction of a series of fusion peptides with which binding affinities and consequently activity can be manipulated to achieve optimal clinical results. [Commerialization of sequences discovered using Ph.D.™, a trademark of New England Biolabs, Inc., may require a liscence from Dyax Corp.]

Testing the Hypothesis

Branched and linear peptides containing the mimetic sequence were synthesized by solid-phase methods using standard Fmoc side chain protection. The branched peptide was constructed on a poly-lysine core consisting of 4 branches containing a linker

sequence of GGGS and a dansylated C-terminal cysteine. The linear peptide also contained the linker sequence GGGS, a dansyl group and was C-terminally linked to a polystyrene bead. Human monocyte cell line THP-1 and mouse monocyte cell line WEHI-3 have been purchased for macrophage activation assays. Assays for activation will include oxidative burst assays, cytochrome C reduction assays, and fluorescence microscopy. In addition, N-terminally linked cross-linking reactive groups will be appended to the linear peptide for immunoprecipitation assays. The peptides will be crosslinked to the macrophage lectin receptor during activation and the immunoprecipitated complex will be sequenced by mass spectrometry. Identification of the receptor may lead to additional patent coverage.

For *in vivo* production of a GalNAc peptide mimetic fusion protein, panning of a C7C Phage Display Peptide Library kit based on combinatorial library of random 7-mers flanked by a pair of cysteine residues is currently underway. Disulfide constrained peptides will be useful in maintaining the structural integrity of the mimetic. This sequence will be incorporated into the C-terminal loop domain of human Vitamin D-Binding protein and overexpressed in the appropriate host.

(1) Yamamoto N, Naraparaju VR, Srinivasula SM (1995) Structural modification of serum Vitamin D_3-Binding protein and immunosuppression in AIDS patients. AIDS Res Human Retroviruses 11:1373-1378

(2) YamamotoN, Naraparaju VR (1997) Immunotherapy in BALB/c mice bearing Ehrlich ascites tumor with Vitamin D-Binding protein-derived macrophage activating factor. Cancer Res 57:2187-2192

(3) Monvzavi-Karbassi B, Cunto-AmenestyG, Luo P, Kieber-Emmons T (2002) Peptide mimotopes as surrogate antigens of carbohydrates in vaccine discovery. Trends Biotechnol 20:207-14